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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,486	08/31/2006	John S. Yu	22862-0003US1 / 67789-567	6180
26161 7590 05/25/2011 FISH & RICHARDSON P.C. (BO) P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER JUEDES, AMY E	
			ART UNIT 1644	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary

Application No.

10/598,486

Applicant(s)

YU ET AL.

Examiner

AMY JUEDES

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1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 March 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 12-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 12-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/4/11</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's amendment and remarks, filed 3/7/11, are acknowledged.
Claims 1-7 and 12-24 are pending and are under examination.
2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7 and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/38730 (of record), in view of Geiger et al., 2001, and Kalinski et al., 1998 (of record) as evidenced by the material safety data sheet for NS-398 (2008).

As set forth previously, WO 00/38730 teaches a method of treating cancer in a human subject comprising administering a combination of a COX-2 inhibitor and a vaccine to the subject (see page 9, in particular). WO 00/38730 teaches that the method is suitable for treating a wide range of cancers including ependymal tumors, glioblastoma (i.e. glioma or brain cancer), and neuroblastoma (see page 10, in particular). WO 00/38730 teaches that the vaccine includes agents that induce the patients immune system to mount an immune response against the tumor, and that the COX-2 inhibitors include celecoxib and N-[2-(cyclohexyloxy)-4-nitrophenyl] methanesulfonamide (see page 22, 42, and 52, in particular). As evidenced by the material safety data sheet, N-[2-(cyclohexyloxy)-4-nitrophenyl] is NS-398. WO 00/38730 teaches administering a single dose of the COX-2 inhibitor at a concentration of 1mg to about 1000 mg (see page 66, in particular). WO 00/38730 also teaches that COX-2 inhibitors function to treat cancer by inhibiting the COX-2 activity of neoplastic lesions, since the products of COX-2 activity, such as

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PGE2, stimulate cancer cell growth and inhibit immune surveillance (see page 36-38, in particular). WO 00/38730 also teaches that the combination therapy can maximize the therapeutic effect of each of the compounds (i.e. the COX-2 inhibitor enhances the effect of the vaccine, see page 11-12, in particular).

WO 00/38730 does not teach administering a dendritic cell as the vaccine component.

Geiger et al. teach that dendritic cells can be used as a vaccine to induce an immune response and treat cancer in human patients, including those with neuroblastoma or primitive neuroectodermal tumor (see page 8515, in particular). Geiger et al. teach that the administered dendritic cells are immature dendritic cells that have been pulsed with tumor lysate in vitro (see page 8515, in particular). Geiger et al. teach administering 1×10^7 dendritic cells (see page 8515, in particular). Geiger et al. also teach that injected dendritic cells may mature in vivo after administration (see page 8517, in particular). Geiger et al. also teach that IFN-gamma production (i.e. a Th1 response) correlates with vaccine efficacy (see page 8518, in particular). With respect to claims 12 and 13 of the instant application, it is noted that the instant specification does not specifically define the terms "primed" or "unprimed". Rather, the specification on page 12 states that dendritic cells can be "primed" ex vivo by conventional methods for example loading with a tumor cell lysate. The specification further states that "unprimed" dendritic cells include those dendritic cells that do not rely upon acquisition of tumor tissue as a protein source, and the subsequent culturing therewith. Thus, the specification only gives antigen pulsed dendritic cells as a specific examples of "primed" dendritic cells, and dendritic cells not cultured with antigen as a specific example of "unprimed" dendritic cells, but does not specifically define the scope of the terms "primed" and "unprimed". It is noted that Geiger et al. teach pulsing the dendritic cells with tumor cell lysate, and thus said dendritic cells can be considered "primed" with antigen. However, Geiger et al. also teach that the dendritic cells are immature dendritic cells that have not been actively matured in culture with specific maturation factors (see page 8516, in particular). Given the broadest reasonable interpretation of the term "unprimed" it can be considered to encompass immature dendritic cells which have not been treated or primed in vitro with maturation factors (i.e. the dendritic cells of Geiger et al. are "unprimed" with respect to maturation factors).

Kalinski et al. teach that PGE-2 impairs IL-12 production and Th1 priming capacity of dendritic cells if it is present when dendritic cells are undergoing maturation (see page 2807 and 2808, in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a dendritic cell as the vaccine, as taught by Geiger et al., in the method of treating cancer of WO 00/38730. The ordinary artisan at the time the invention was made would have been motivated to do so and have a reasonable expectation of success, since Geiger et al. teach that dendritic cells can be used as a vaccine for treating cancer. Furthermore, WO 00/3870 teaches that inhibition of COX-2 decreases PGE-2 production, and Kalinski et al. teach that PGE-2 inhibits IL-12 production and TH1 priming by dendritic cells. Thus, the ordinary artisan would be motivated to administer a combination of a COX-2 inhibitor with a dendritic cell vaccine to inhibit PGE-2 production in order to enhance IL-12 production and Th1 priming by the dendritic cells in vivo.

Applicant's arguments filed 3/7/11 have been fully considered, but they are not persuasive.

Applicant argues that WO 00/38730 discloses administering a COX-2 inhibitor in combination with a vaccine, but does not disclose the rationale as to why inhibition of

COX-2 would be useful in combination with a vaccine. Applicant notes that Geiger discloses administering dendritic cells but does not disclose the use of COX-2 inhibitors. Applicant further argues that Kalinski does not remedy the deficiencies of WO 00/38730 and Geiger et al. since there is no teaching or suggestion as to the effect of PGE or COX-2 inhibitors on exogenously administered dendritic cells.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). As noted above, WO 00/38730 discloses combining a COX-2 inhibitor with a vaccine. In contrast to Applicant's assertions it is noted that WO 00/38730 teaches that the COX-2 inhibitor functions to inhibit the COX-2 activity of neoplastic lesions, such as PGE₂ induction which stimulates cancer cell growth and inhibits immune surveillance. Thus, it would be readily apparent that COX-2 inhibitors would increase the immune recognition of tumor cells after vaccination. It would be obvious to administer a COX-2 inhibitor, as taught by WO 00/38730, along with a dendritic cell vaccine of Geiger et al., in order to increase tumor immune surveillance by the vaccine induced immune cells. Furthermore, the ordinary artisan would be motivated to specifically combine a dendritic cell vaccine with a COX-2 inhibitor, since Kalinski et al. teach that PGE-2 (which is suppressed after COX-2 inhibition) is detrimental to dendritic cells since it impairs IL-12 production and Th1 priming capacity of dendritic cells.

Applicant further argues that the antigen pulsed dendritic cells of Geiger et al. are not "unprimed", since the instant specification makes clear that the primed dendritic cells are those that have been exposed to antigens, citing paragraphs 44-45.

As an initial matter, only claim 13 is limited to "unprimed" dendritic cells. The instant specification discloses dendritic cells that have not been pulsed with antigen as a specific example of "unprimed" dendritic cells. However, the specification does not define the scope of the term "unprimed", and the claims are not limited to "unprimed" dendritic cells that have not been pulsed with antigen. Furthermore, the ordinary definition of "priming" includes the act of making something ready for use. Thus, the

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broadest reasonable interpretation of the term "unprimed" dendritic cells would also include those that have not been actively matured by in vitro culture (i.e. "made ready" for activating T cells).

3. Claims 1, 3-7, 12, 14-15, 17-22, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/38730 (of record), in view of U.S. Patent 7,240,982 and Zeidler et al., 2000, as evidenced by the material safety data sheet for NS-398 (2008).

As set forth previously, The '982 patent teaches a GDOX gene that is overexpressed in glioblastoma tumors, and the use of GDOX as a tumor antigen for vaccine therapy of cancer. The '982 patent teaches a method of treating cancer comprising administering a dendritic cell vaccine expressing a GDOX tumor polypeptide (see columns 21-22). The '982 patent teaches administering dendritic cells that have been matured by culture with cytokines (see column 22, in particular). The '982 patent teaches treating human subjects, and that the method induces an anti-tumor T cell immune response (see columns 21-22, in particular). The '982 patent teaches that the dendritic cells are loaded with the GDOX polypeptide, or with a DNA encoding the polypeptide (i.e. "primed", see column 22, in particular).

The '982 patent does not teach administering a COX-2 inhibitor.

WO 00/38730 teaches a method of treating cancer in a human subject comprising administering a combination of a COX-2 inhibitor and a vaccine to the subject (see page 9, in particular). WO 00/38730 teaches that the method is suitable for treating a wide range of cancers including ependymal tumors, glioblastoma (i.e. glioma or brain cancer), and neuroblastoma (see page 10, in particular). WO 00/38730 teaches that the vaccine includes agents that induce the patients immune system to mount an immune response against the tumor, and that the COX-2 inhibitors include celecoxib and N-[2-(cyclohexyloxy)-4-nitrophenyl] methanesulfonamide (see page 22, 42, and 52, in particular). As evidenced by the material safety data sheet, N-[2-(cyclohexyloxy)-4-nitrophenyl] is NS-398. WO 00/38730 teaches administering a single dose of the COX-2 inhibitor at a concentration of 1mg to about 1000mg (see page 66, in particular). WO 00/38730 also teaches that COX-2 inhibitors function to treat cancer by inhibiting the COX-2 activity of neoplastic lesions, since the products of COX-2 activity, such as PGE₂, stimulate cancer cell growth and inhibit immune surveillance (see page 36-38, in particular). WO 00/38730 also teaches that the combination therapy can maximize the therapeutic effect of each of the compounds (i.e. the COX-2 inhibitor enhances the effect of the vaccine, see page 11-12, in particular).

Zeidler et al. teach that PGE₂ production by tumor cells can contribute to immune evasion by downregulating MHC expression in the tumor cells and by inhibiting the function of tumor infiltrating T cells (see page 666, in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to further administering a COX-2 inhibitor, as taught by WO 00/38730, in the method of dendritic cell vaccination taught by the '982 patent. The ordinary artisan at the time the invention was made would have been motivated to do so and have a reasonable expectation of success, since WO 00/3870 teaches that COX-2 inhibitors decreases PGE-2 production, and can be used in combination with a vaccine to maximize the therapeutic effect of

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the vaccine. Additionally, Zeidler et al. teach that tumor derived PGE-2 decreases tumor MHC expression and inhibits T cell function. Thus, the ordinary artisan would be particularly motivated to administer a COX-2 inhibitor with the dendritic cell vaccine of the '982 patent in order to inhibit PGE-2 production by the tumor cells, and hence render the induced T cells more effective in mediating anti-tumor activity in vivo.

Applicant's arguments filed 3/7/11 have been fully considered, but they are not persuasive.

Applicant argues that WO 00/38730 discloses administering COX-2 in combination with a vaccine, but does not disclose the rationale as to why inhibition of COX-2 would be useful in combination with a vaccine. Applicant notes that the '982 patent discloses administering dendritic cells but does not disclose the use of COX-2 inhibitors. Applicant further argues that Zeidler et al. do not disclose that tumor derived PGE-2 decreases tumor MHC expression and inhibits T cell function. Rather, Applicant argues that Zeidler et al. teach that PGE2 causes downregulation of CCR5 and Mac-1 on monocytes without effecting MHC.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). As noted above, WO 00/38730 discloses combining a COX-2 inhibitor with a vaccine, and discloses that the COX-2 inhibitor functions to suppress PGE-2, thereby increasing immune surveillance of the tumor. Furthermore, the '982 patent teaches the use of mature dendritic cells as a vaccine for inducing a T cell response to treat cancer. It would be obvious to administer a COX-2 inhibitor, as taught by WO 00/38730, along with a dendritic cell vaccine of the '982 patent, to inhibit to COX-2 activity of neoplastic cells, thereby inhibiting PGE2 and increasing immune surveillance.. Furthermore, regarding the teachings of Zeidler et al., it is noted that the reference teaches that PGE-2 functions to cause downregulation of CCR5 and Mac-1, but not MHC on *monocytes*. However, the reference also teaches that tumor immune evasion involves downregulation of MHC, and that PGE-2 has been known to have an immunosuppressive effect for several years. Zeidler et al. also teach that blockade of PGE2 synthesis improves tumor infiltration by immune cells and reduces tumor cell

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growth. Zeidler et al. also teach tumor derived PGE2 induces production of IL-10 and TNF, which inhibit immune cell function and T cell proliferation (see page 666, in particular). The '982 patent specifically teaches that the dendritic cell vaccine functions to treat cancer by inducing anti-tumor T cell responses. Furthermore, Zeidler et al. teach that tumor derived PGE-2 is immunosuppressive and can inhibit immune cell infiltration into tumors, inhibits immune cell function and T cell proliferation. Therefore, the ordinary artisan would be further motivated to administer a COX-2 inhibitor in combination with a dendritic cell vaccine, since it would inhibit the immunosuppressive effects of PGE-2 on the anti-tumor T cell response induced by the mature dendritic cell vaccine.

4. Claims 2, 13, 16, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/38730 (of record), U.S. Patent 7,204,982 and Zeidler et al., 2000, as evidenced by the material safety data sheet for NS-398 (2008), as applied to claims 1, 3-7, 12, 14-15, 17-22, and 24 above, and further in view of U.S. Patent 6,300,090 and Kikuchi et al., 2001 (of record).

As set forth previously, The combined teachings of WO 00/38730 (of record), U.S. Patent 7,240,982 and Zeidler et al., 2000, are discussed above.

They do not teach “unprimed” dendritic cells or administering from 10^5 to 10^7 dendritic cells.

The '090 patent teaches that freshly isolated mature dendritic cell are suitable for use as a vaccine after antigen delivery in vitro (see column 8, in particular).

Kikuchi et al. teach administering $2-8 \times 10^6$ dendritic cells as a vaccine for treating glioma.

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of the '090 patent to the method of vaccination made obvious by WO 00/38730, the '982 patent, and Zeidler. Selecting from the known dendritic cell populations suitable for vaccination would involve choosing among a finite number of predictable options which could be pursued with a reasonable expectation of success. A person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense (see *KSR International Co. V. Teleflex Inc* 82 USPQ2d 1385). Furthermore, freshly isolated mature dendritic cells, as taught by the '090 patent can be considered “unprimed” since they have not been matured (i.e. primed) with cytokines in vitro. Additionally, it would have been obvious to optimize the number of administered cells, and the claimed dendritic cells numbers are well within the purview of the ordinary artisan, as taught by Kikuchi et al. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation (see *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235).

Applicant's arguments filed 3/7/11 have been fully considered, but they are not persuasive.

Applicant argues that neither the '090 patent nor Kikuchi et al. remedy the defects discussed above.

However, the instant claims are obvious for the reasons set forth above.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 23 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for treating cancer in a human comprising administering a mature dendritic cell that has been primed with antigen,
does not reasonably provide enablement for:

a method for treating cancer in a human comprising administering a mature dendritic cell that is antigen "unprimed".

As set forth previously, The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03) The MPEP further states that physiological activity can be considered inherently unpredictable.

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The instant claims is drawn to a method for treating cancer comprising administering a mature "unprimed" dendritic cell. The specification on page 12 teaches that one example of "unprimed" dendritic cells are those that have not been loaded in vitro with antigen. Thus, the claimed method encompasses administering mature dendritic cells which have not been loaded with antigen. The state of the art is such that immature dendritic cells can be administered to the site of a tumor, where they can acquire tumor antigen in situ for stimulating a protective T cell response. However, mature dendritic cells lose their ability to take up antigens (see Tanaka et al., 2005). Thus, it would be highly unpredictable as to whether a mature dendritic cells that has not been loaded with antigen, as is encompassed by the instant claim, would be effective for inducing a T cell response and treating cancer.

Thus, based on the unpredictability of the art, the instant specification must provide a sufficient an enabling disclosure commensurate in scope with the instant claims. The specification on pages 12-13 teaches that "unprimed" dendritic cells are intended to acquire and process the tumor antigens in vivo to be effective for treating cancer. However, as noted above, only immature dendritic cells are capable of processing antigen. The specification does not provide any guidance for producing mature dendritic cells that are capable of acquiring and processing tumor antigens after administration. Thus, based on the unpredictability of the art and the lack of guidance provided by the instant specification, it would require undue experimentation to practice the method as claimed.

Applicant's arguments filed 3/7/11 have been fully considered, but they are not persuasive.

Applicant argues that claim 16 does not recite treating with an unprimed mature dendritic cell.

The original rejection cited claim 16 in the heading, which was an obvious typographical error. The body of rejection makes clear that the non-enabled subject matter is a method comprising administering a mature "unprimed" dendritic cells, which is the exact subject matter recited in claim 23. The heading of the rejection has been changed to correct this obvious typographical error.

6. No claim is allowed.

7. **ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amy E. Juedes

Patent Examiner

Technology Center 1600

/Amy E. Juedes/

Primary Examiner, Art Unit 1644